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Scientific Accomplishments Report

Genetic and biochemical data indicate that the genes, the carriers of hereditary information, are composed of deoxyribosenucleic acid (DNA). The relation between specific genes and specific proteins has been demonstrated in many laboratories. Thus, in any organism, the presence of a given gene will be expressed by the synthesis of a particular protein of definite structure (i.e., linear arrangement of amino acids). It is generally believed that the linear array of monodeoxynucleotide units in DNA reflects a code which directs the sequence of amino acids in the related protein. Various experiments also suggest that this transfer of information from DNA to protein is mediated by a third material, namely, ribosenucleic acid (RNA).

Neither the precise mechanism of protein biosynthesis nor the specific role of RNA in that process has been definitively described. However, it is widely believed that the first steps in the process are 1) the activation of amino acids by specific enzymes and 2) the enzymatically catalyzed transfer of the amino acids to RNA. These two reactions have been described. The RNA found in solution in the cell sap functions in this way and there is evidence that distinct RNA chains (transfer RNA) exist for the different amino acids. Further, it is believed that the sequence of nucleotide units in a particular transfer RNA chain determines that chain's specificity for a given amino acid.

During the past year, in collaboration with Dr. Giulio L. Cantoni of the National Institute of Mental Health, we studied the structure of the transfer RNA. As a result of these studies several interesting and significant features of the transfer RNA have been elucidated. The work was carried out on samples of transfer RNA containing chains specific for a variety of amino acids. The general structure of RNA may be written pNpNpNpN.....pNpNpN (where N represents purine or pyrimidine ribonucleosides and p represents phosphate groups). Chemical chain length studies and analysis in the ultracentrifuge indicate that the number of N moieties in transfer RNA is about 100. We have found that all the transfer RNA molecules in the mixture have the same nucleotide at the left-hand end of the chain (as written above) and that this residue is 5'-guanylic acid. Similarly, the extreme right-hand side of the chain was found to be either adenosine or cytidine. These latter findings are consistent with work in several other laboratories ~~which~~ that indicates that a terminal.....pCpCpA sequence is required for transfer RNA to bind amino acids (C and A stand for cytidine and adenosine moeities, respectively). The same sequence holds for all the amino acids. Thus we may write a somewhat more specific structure for transfer RNA, namely pGpNpNpN .....pNpCpCpA. It is of interest that the two ends of all the chains are the same.

One can conclude from these findings that the specificity of a particular transfer RNA for a given amino acid must be determined somewhere in the internal portion of the chain.

Several interesting facts were found when the total nucleotide content of the transfer RNA was determined. The five main nucleotide residues are present in the following relative amounts: Adenylic acid, 17, uridylic acid, 17, guanylic acid, 31, cytidylic acid, 29, and 5-ribosyluracil monophosphate, 3. The transfer RNA is thus characterized by a very high content of the recently discovered nucleotide, 5-ribosyluracil monophosphate. Other types of RNA have almost negligible amounts of this compound. The significance of the high quantity of 5-ribosyluracil in transfer RNA is, at present, unknown. A second point of interest is the near equivalence of adenylic and uridylic acid on one hand, and cytidylic and guanylic acid on the other. Total cellular RNA does not show this relation. DNA does, however, have a similar equivalence of nucleotides and this led us to investigate the possibility that transfer RNA has a hydrogen-bonded double-helical secondary structure similar to that of DNA. In these experiments we studied the reactivity of transfer RNA in specific chemical and enzymatic procedures. The results permit certain tentative conclusions concerning the secondary structure of the RNA. Thus, although we do not believe that the secondary structure of transfer RNA is like that of DNA, regions of intermolecular or intramolecular hydrogen bonding probably exist. We are now investigating this hypothesis further.

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